Allergy Abstracts

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Asthma and Hay Fever

Symptoms of Hay Fever Caused by Algae. Heise, H. A.: Ann. Allergy **9**: 100, 1951.

Oscillatoriaceae, a subgroup of the blue-green algae (Myxophyceae) has been shown to be a cause of hay fever symptoms in August and September. The author reports another subgroup of Myxophyceae, Genus: Microcystis, as a possible cause of hay fever. Simultaneous tests with both algae produced identical skin reactions in each of 10 susceptible persons tested. Approximately 50 other persons were tested and failed to react to either antigen. The author postulates the presence of a similar antigen in both subgroups.

M. Scherr

The Mushroom Fly as a Cause of Bronchial Asthma. Truitt, G. W.: Ann. Allergy **9**: 513, 1951.

The mushroom fly (Aphiochaeta agarici) has been found to be a cause of bronchial asthma in the areas where mushrooms are grown. Extracts of this antigen have been used for the demonstration of hypersensitiveness by direct and passive transfer tests. Treatment with the fly extract has been satisfactory.

M. Scherr

Toxic Hepatitis Caused by Prolonged Inorganic Arsenic Intake: Studies on Liver Dysfunction—VII. Pelner, L., and Waldman, S.: New York State J. Med. **51**: 2511, 1951.

A 54-year-old man with bronchial asthma of 7 years' duration had been taking the arsenic treatment for one and one-half years. He stated that he

had experienced fairly good results at first, but that the medication afforded less relief during the last few months. The complaints for which he consulted his physician were pain in the right upper quadrant of the abdomen, belching, and a sense of fullness. Physical examination at this time revealed a chronically ill patient with a peculiar pallor and feel to the skin. Many areas of the skin showed a brownish discoloration resembling freckles. The liver was enlarged 4 fingers below the costal arch and was tender. The icterus index was 11.0, total proteins 6.8 Gm. per cent, and the albumin globulin ratio was 1.7:1. The urine was positive for urobilinogen in a dilution of 1:200 and showed a faint trace of albumin and a rare hyaline cast. A 24 hour specimen of 1,655 c.c. of urine had an arsenic content of 1.24 mg. (normal, 0 to .06 mg. per liter). The patient was placed on a lipotropic agent and the arsenic formula was discontinued. There was a rapid improvement in gastrointestinal symptoms. During the following 2 months, the liver gradually diminished in size and the arsenic content of the urine diminished. The asthma became worse after the offending medication was discontinued, but could be controlled with aminophylline and epinephrine.

The authors suggest that arsenic may be beneficial in asthma by interfering with the activity of enzymes having the S H group and so "occupy" one or more of the liver functions. This frequently results in a toxic hepatitis. B. S.

Remissions in Bronchial Asthma and Hypertrophic Pulmonary Emphysema. Barach, A. L.: J. A. M. A. **147**: 730, 1951.

Epinephrine, ephedrine, and aminophylline ordinarily provide excellent means for controlling acute attacks of bronchial asthma. When the patient becomes refractory to these medications, it becomes necessary to curtail their use in order to effect a remission and restore the patient's sensitiveness to these drugs. Medications which may accomplish such an effect include demerol, potassium iodide, paraldehyde, and ether, and the inhalation of nebulized epinephrine or racemic epinephrine. Inhalation of helium and oxygen alone or in conjunction with nebulized epinephrine often produces a marked increase in vital capacity. Other procedures which may be employed with success are typhoid-induced fever therapy, penicillin alone or in combination with the broad spectrum antibiotics, and bronchoscopy or bronchial aspiration while the patient is under ether anesthesia. Respiratory exercises, abdominal belts, and pneumoperitoneum in conjunction with the belts may give relief particularly in the bronchospastic type of chronic hypertrophic pulmonary emphysema. ACTH and cortisone are particularly useful in treating patients who experience an exacerbation of asthma following acute infections or exposure to pollen. F.

Treatment of Chronic Pulmonary Disease With Intermittent Positive Pressure Breathing: Evaluation by Objective Physiological Measurements. Motley, H. L., and Tomashefski, J. F.: Arch. Indust. Hyg. & Occ. Med. **5**: 1, 1952.

Treatment with intermittent positive pressure breathing affords a means of rehabilitating chronic pulmonary invalids to a state where they can carry on gainful occupations. Employing a commercially available Bennett apparatus specifically designed for giving IPPB treatments, the authors were able to provide subjective and objective relief to a majority of 300 cases suffering from emphysema and pulmonary fibrosis with dyspnea. Incorporated in the apparatus is a nebulizer through which a bronchodilator drug may be delivered to the patient while the IPPB treatment is being carried out. Sec-

ondary symptoms and electrocardiographic changes often caused by these bronchodilators are avoided by controlling the rate of nebulization and by using oxygen for operating the apparatus. Severely dyspneic emphysematous patients received greatest benefit from treatments given in the early morning, whereas asthmatics seemed to find the bedtime treatment most beneficial. Bronchospasm is a significant factor in the production of dyspnea in patients with fibrosis and emphysema. The increase in maximum breathing capacity noted after the IPPB-bronchodilator treatment is believed to be due to elimination of bronchial spasm. Pulmonary function studies taken before and after a course of therapy revealed that the measurable objective changes are primarily related to the volume of, and resistance to, air moving in and out of the lungs, i.e., vital capacity, maximum breathing capacity, and instantaneous inspiratory and expiratory flow rate patterns. The treatments actually produce an expectorant-like action because the peak expiratory flow is greater than the peak inspiratory velocity and promotes an outward flow of secretions. Several months of treatment may be required for beneficial effects to become manifest in severely ill patients. The breathing exercises are contraindicated in cases of recent hemoptysis and recent spontaneous pneumothorax. F.

Treatment of Bronchial Asthma With Pregnenolone Acetate. Lima, A. O.: Ann. Allergy **9**: 31, 1951.

Pregnenolone has been shown to have an adrenocortical activity similar to desoxycorticosterone. The favorable clinical results obtained with structurally related compounds in rheumatoid arthritis suggested a trial of these compounds in other allergic diseases. Twenty patients with allergic bronchial asthma were treated with pregnenolone acetate in dosage of 400 mg. daily for a period of 15 days. The author found the drug had no effect on bronchial asthma or on skin reactions to diagnostic tests with food and inhalant allergens. M. Scherr

Norisodrine by Aerohalor in Asthma. Kaufman, R. E., and Farmer, L.: Ann. Allergy **9**: 89, 1951.

Norisodrine (isopropylarterenol) dust was administered by Aerohalor to 63 patients with asthma and to one patient with an allergic cough. The results were reported to be excellent in 39 cases, good to fair in 13, and poor in 12. Side effects were mild and transitory and continued use produced no diminution in therapeutic effect in most of the cases. M. Scherr

Observations on the Action of Khellin in Attacks of Bronchial Asthma. Derbes, V. J., White, R. V., Teverbaugh, J., Vaughan, D. D., and Weaver, N. K.: Ann. Allergy **9**: 354, 1951.

Khellin was administered in 100 mg. doses to 45 patients with bronchial asthma. Of 20 patients who received the drug intramuscularly, good or excellent results were experienced by 12 and slight or negative results by 8. Twenty-five patients took the drug orally and of these 14 had good or excellent results. A low incidence of side reactions was encountered. Khellin in the dosage given had little effect on blood pressure. M. Scherr

Norisodrine Sulfate (25 Per Cent) Dust Inhalation in Severe Asthma. Swartz, H.: Ann. Allergy **8**: 488, 1950.

Norisodrine sulfate dust inhalation proved effective in relieving the symptoms of 11 of 12 patients with severe asthma of the extrinsic, intrinsic, or com-

bined types. Most of these patients had required frequent injections of epinephrine or aminophylline, some were epinephrine-fast. Side reactions due to Norisodrine were minimal. Four patients with mild asthma failed to obtain relief from this drug. It was suggested that the efficacy of Norisodrine is based primarily on its bronchodilating effect which is maximal in chronic asthma where bronchospasm is a more pronounced factor than broncho-mucosal edema. E. W.

Dermatology

Acquired Contact Sensitivity to Chloromycetin. Robinson, H. M., Jr., Zeligman, I., Shapiro, and A., Cohen, M. M.: J. Invest. Dermat. **17**: 205, 1951.

From a group of 70 individuals who had been treated with 1 per cent Chloromycetin cream, 2 patients developed an edematous vesicular dermatitis after prolonged application of the medicant. As soon as the drug was stopped, the rash quickly cleared in each case. When subsequently tested, the patients showed positive patch reactions to Chloromycetin cream and to Chloromycetin powder, but a negative reaction to the cream base. R. W.

Further Experiments on the Formation of Skin Tolerance to Antihistaminic Drugs. Monash, S., and Guiducci, A.: New York State J. Med. **51**: 1309, 1951.

Patients were given an antihistaminic drug in the usual dosage 3 times daily for one week. Double the usual dose of a different antihistaminic drug was then given. The threshold skin reaction to histamine phosphate was then determined by iontophoresis at varying intervals during the 4-hour period after the administration of the second drug. In the 2 cases presented, the threshold concentration of histamine increased following the second drug, thus demonstrating an antihistaminic effect. However, when this drug was administered daily during the next week and the histamine tests were repeated after a double dose of the same drug, the threshold concentration of histamine remained unchanged. It was concluded that increased tolerance of the skin to an antihistaminic drug is produced after use for one week. However, this increased tolerance does not necessarily extend to other antihistaminic drugs. It is suggested that patients on antihistaminic therapy change drugs at weekly intervals. B. S.

Chromate Dermatitis in Railroad Employees Working With Diesel Locomotives. Winston, J. R., and Walsh, E. N.: J. A. M. A. **147**: 1133, 1951.

Sodium bichromate, a constituent of Diesel locomotive radiator fluid, was found to be the cause of 6 cases of contact dermatitis among 200 workers exposed to this material. The dermatitis responded slowly to treatment consisting of wet dressings, bland ointments, and minimal superficial x-ray therapy. Since sensitivity to chromate may first develop after comparatively long periods of exposure and once developed tends to increase rather than decrease in severity, pre-employment patch testing is a worthless procedure. F.

The Effect of Cortisone on Experimentally-Induced Contact Dermatitis. Baldridge, G. D., and Kilgman, A. M.: J. Invest. Dermat. **17**: 257, 1951.

Contact dermatitis to 2-4 dinitrochlorbenzene was induced in guinea pigs. One group of animals was given 10 mg. of cortisone intramuscularly daily for a short period prior to and immediately following initial exposure to

the chemical. A second group of animals was given daily intramuscular injections of 10 mg. of cortisone during the entire period of sensitization. A third group was given one intramuscular injection of 10 mg. of cortisone 24 hours prior to the eliciting exposure. The control group did not receive cortisone therapy. All patch testing was done with an antigenic concentration which had proved to be nonirritating. When the results were tabulated, there was no difference between the treated and the control groups in the incidence of positive patch test reactions. The authors stress the importance of more careful evaluation of the results obtained from the use of ACTH or cortisone in the treatment of eczematous contact dermatitis. R. W.

Local Hemorrhagic-Necrotic Skin Reaction Following Penicillin. Review of Literature and Case Report. Rubens, E.: J. Pediat. **38**: 630, 1951.

Following an intramuscular injection of 300,000 units of procaine penicillin in peanut oil for an acute pharyngitis, a 6-month-old infant developed an immediate local reaction. The patient had received a similar dose of the same drug 6 weeks previously for an upper respiratory infection, without ill effects. Within one hour, the site of the second injection became red, hot, swollen, and tender. Later there was purplish discoloration, hemorrhagic streaking, and eventually, necrosis, and sloughing. Complete healing took place after 6 weeks of active local treatment. Positive skin reactions were obtained to tests with procaine penicillin G and potassium penicillin G. The authors review the literature on such reactions and discuss the Arthus reaction, the Shwartzman phenomenon, and embolia cutis medicamentosa as possible diagnoses of the reaction in this patient. J. S.

Use of Neomycin in Dermatology. Kile, R. L., Rockwell, E. N., and Schwarz, J.: J. A. M. A. **148**: 339, 1952.

Only one proved instance of contact sensitivity to neomycin was found in 869 cases, including those given provocative patch tests. Skin lesions, indicative of irritation but not confirmed by positive patch tests, occurred in several cases. H.

Occupational Dermatoses in Physicians. Epstein, E.: J. A. M. A. **147**: 1751, 1951.

Contact dermatitis caused by scrubbing, local anesthetics, rubber gloves, antiseptics, and antibiotics is the most frequently encountered occupational injury suffered by physicians. Infections, accidentally acquired from patients, and radiodermatitis occur less commonly. F.

Some Endocrine Aspects of Skin Sensitization and Primary Irritation. I. Observations on the Influence of Cortisone on Cutaneous Irritation and Sensitization Induced by Various Chemical Compounds. Nitzen, A.: J. Invest. Dermat. **18**: 7, 1952.

Guinea pigs were either sensitized to 2, 4-dinitrochlorbenzene or exposed to various primary irritants. When cortisone was administered intramuscularly during the entire period of sensitization to 2, 4-dinitrochlorbenzene but discontinued prior to the test dose, there was a definite diminution in the specific response obtained when compared with a saline-treated control group. One dose of cortisone injected 1 hour prior to the challenging test or exposure

of the animals to the stress of refrigeration for from 4 to 6 hours was found to delay the specific response. Passive transfer of 2, 4-dinitrochlorbenzene sensitivity in guinea pigs was unaffected by cortisone therapy when the drug was administered during the entire period of sensitization or just prior to the transference. There was a slight but definite diminution in the response obtained following the application of croton oil in the cortisone-treated animals. A similar difference in response but to a lesser extent was also noticed in the cantharidin- and colchicine-exposed animals. Following the application of croton oil or 2, 4-dinitrochlorbenzene to areas previously prepared by the injection of cortisone intracutaneously, it was not possible to find any macroscopic or microscopic difference in the reactions obtained. Large doses of cortisone administered parenterally or prolonged exposure to cold did not prevent sensitization with 2, 4-dinitrochlorbenzene. It is suggested that cortisone must be given systemically in order to affect vascular tissue and that the relief which occurs in skin reactions following epicutaneous exposure to chemicals probably results from the action of cortisone on the blood vessels.
R. W.

The Local Effect of 17-Hydroxycorticosterone-21-Acetate (Compound F) on the Diagnostic Patch Test Reaction. Goldman, L., Preston, R., and Rockwell, E.: J. Invest. Dermat. **18**: 89, 1952.

Following an intracutaneous injection of from 0.1 to 0.5 mg. of 17-hydroxycorticosterone-21-acetate, patients known to be sensitive to mercury, nickel, tar, Rhus toxin, adhesive tape, and turpentine were patch tested over the prepared sites. No mention was made as to the length of time which elapsed between the injection and the application of the specific excitant. Cholesterol and cortisone were used for control preparatory injections. Except in those patients sensitive to Rhus toxin, a marked diminution in response was obtained in the areas previously prepared with Compound F. In one patient who was sensitive to mercury, the inhibitory effect lasted for at least 5 days. This inhibition of allergic activity extended well beyond the area of actual injection. Skin responses to primary irritants such as 100 per cent turpentine and 5 per cent cantharidin were not affected. The authors are unable at present to offer an explanation for the results obtained. R. W.

Comparing the Irritant Action of Soaps. Schwartz, L.: Ann. Allergy **8**: 530, 1950.

A standardized method of patch testing was used to compare the relative skin irritant properties of soaps. A new deodorant soap containing Hexachlorophene and perfume was compared with a base soap and with a deodorant soap in general use for many years. Two hundred subjects were patch tested with 3 per cent solutions of these soaps according to the author's technique. When the patches were removed in 24 hours, it was found that 90 per cent of the subjects reacted to all 3 soaps. This was attributed to primary skin irritation. A 2 per cent solution of the soaps likewise was irritating. When the subjects were retested 2 weeks later with 1 per cent solutions, 46 per cent reacted to the base soap, 17 per cent to the Hexachlorophene soap, and 51 per cent to the control deodorant soap. It is suggested that the superfatting of the soap by the addition of the essenial oils of the perfume and by the Hexachlorophene might have reduced the irritating properties. Since these experiments, several million cakes of the new deodorant soap have been sold with no proved cases of sensitization having been reported. E. W.

Keloid Resulting From a Positive Patch Test. Dalton, J. E.: Arch. Dermat. & Syph. **65**: 53, 1952.

Occupational contact with antibiotics resulted in a generalized contact type of dermatitis in a white, fair-skinned, 22-year-old woman. Patch tests performed with penicillin and streptomycin gave negative reactions, but a severe positive reaction was obtained at the site tested with patulin. Within one month after avoiding the offender, the lesions cleared. A few months later, itching developed at the site of the positive patch test and within a year a dime-sized, irregularly shaped, solid skin tumor developed at the site. This was excised and was diagnosed histologically as fibrosis of the dermis resembling a keloid. C.

Otorhinology and Ophthalmology

The Effect of ACTH and Cortisone on the Upper Respiratory Tract. Bordley, J. E.: New York State J. Med. **51**: 2636, 1951.

Complete examination of the upper respiratory tract of patients under ACTH or cortisone therapy for various diseases, other than respiratory allergic conditions, revealed several uniform changes. There was a decrease in the nasal mucopurulent discharge and the nasal mucosa appeared healthier. Atrophic areas, crusts, and ulcers tended to disappear. The lymphoid tissue in the nasopharynx developed an orange pink color, crypts in the lymphoid tissue became more prominent, and discharges over the tissue were reproduced and lost their purulent character. Patients, with upper respiratory allergic states under ACTH or cortisone therapy, showed a marked loss of nasal mucosal edema with the development of a deeper color and a reduction of nasal discharge. Polyps lost their translucent appearance and either became very small or disappeared after about 2 weeks of therapy. Polypoid changes of the nasal mucosa also tended to disappear. The thickening of the mucous membranes and polyps in the accessory nasal sinuses, as seen on x-ray, showed a definite diminution under hormone therapy. ACTH was more effective in producing these changes than cortisone. There appeared to be a correlation between the initial eosinopenic response after onset of therapy and the beginning of mucosal and polypoid changes. Signs and symptoms of allergic rhinitis and polyps usually returned in a period varying from 2 weeks to 3 months after the hormone was discontinued.

Several cases of oral and nasal pemphigus responded well to ACTH therapy, but lesions returned rapidly upon withdrawal of the hormone. Two patients with Ménière's disease responded to ACTH with a reduction in unsteadiness, tinnitus, and an improvement in hearing.

Eleven of the 60 ACTH- or cortisone-treated patients developed sinusitis with minimal subjective or objective evidence of the infection. Two of these cases developed blood stream infections. It is suggested that when patients with sinus disease are given this type of therapy, adequate antibiotic coverage should be given to guard against "the silent infection."

Microscopic studies made on nasopharyngeal lymphoid tissue and polyps failed to reveal any uniform changes as a result of hormone therapy during the period of observation. B. S.

Miscellaneous Allergies

Protein Shock From Intravenous ACTH. Wilson, L.: Lancet **2**: 478, 1951.

Two patients who were treated intravenously with a solution containing 20 mg. of ACTH dissolved in 500 c.c. of physiologic saline developed untoward reactions. The infusion was given at a rate which would have required 8 hours to complete the total volume. The ACTH used in both cases was obtained from the same vial. Within 15 minutes following the onset of the therapy, both patients developed reactions consisting of nausea, headache, low back pain, and shaking chills. The intravenous was stopped after approximately 2 mg. had been given, but one hour later both patients went into circulatory collapse and became acutely ill. Eventually, both patients responded to various medications and made uneventful recoveries. Skin tests subsequently performed with the same batch of ACTH were negative. It is stated that the intravenous use of ACTH must not be considered an innocuous procedure and that the hormone should be used intravenously only when absolutely necessary. R. W.

Standardization of Dust Extracts. I. Standardization on the Basis of Equal Molecular Size. Sherago, M.: Berkowitz, B., and Reitman, M.: Ann. Allergy **8**: 437, 1950.

Six dust extracts were assayed for potency according to the method of Rockwell, Thomas, and Wittich. Total nitrogen, phosphotungstic acid precipitable nitrogen, and free alpha amino nitrogen determinations were made. The skin reactivity as measured by the results of intracutaneous tests made on 13 dust-sensitive patients showed no correlation with either the total nitrogen concentration or the phosphotungstic acid precipitable nitrogen concentration. When the phosphotungstic acid precipitable nitrogen figures were divided by the free alpha amino nitrogen values, as proposed by Rockwell et al., it was found that the extracts were of approximately the same molecular size. Although the dust extracts were diluted to the same phosphotungstic acid precipitable nitrogen concentration, there was wide variation in their skin reactivity as determined by direct tests on 16 dust-sensitive patients. These variations in potency were in marked contrast to the findings of Rockwell et al., who reported approximately equal skin reactions to extracts which had been standardized in this manner. It was concluded that methods of standardization based on determinations of nitrogen in any form do not serve as a reliable guide for allergenic potency of dust extracts. E. W.

Effect of Antihistaminics on Experimental Nephritis in Rabbits. Winternitz, W. W., and Hackel, D. B.: Proc. Soc. Exper. Biol. & Med. **78**: 294, 1951.

Acute nephritis was produced in rabbits by a series of injections of duck antirabbit kidney serum. Some of the animals in the group were also treated with various dosage schedues of Pyribenzamine. Judged by the histological picture, the severity of the nephritis was the same in the Pyribenzamine-treated animals and in the untreated controls. The only difference noted in the 2 groups was a delay of from 1 to 3 days in the onset of albuminuria in those treated with Pyribenzamine. B. S.

Bronchography in Iodine Sensitivity. Theodos, P. A.: J. A. M. A. **148**: 1419, 1952.

A patient, who, on several previous occasions, had experienced swelling of the submaxillary glands with fever and urticaria following intrabronchial

instillation of iodized oil, developed symptoms requiring additional bronchographic studies. A test dose of 5 minims of a saturated solution of potassium iodide administered orally produced marked swelling of the submaxillary glands and red blotches on the arms. Cortisone, 20 mg. twice daily for 4 days and then 10 mg. daily for 5 days, was prescribed. On the third day of this regime, intrabronchial instillation of chloriodized oil was attempted by the gravity method. The procedure was unsatisfactory and about 10 c.c. of the oil were swallowed. Slight swelling of the submaxillary glands developed after 5 hours and lasted for several hours. On the following day, the oil was successfully instilled into the bronchi by means of a catheter. A slight iodide reaction lasting several hours occurred, but did not compare in intensity with those previously experienced. F.

Hypersensitivity to P-Aminosalicylic Acid. Klovstad, O.: Tidsskrift f. d. Norsk Laegenforennig. **71**: 759, 1951.

An allergic reaction to para-aminosalicylic acid which occurred on the thirty-third day of treatment is described. Symptoms consisted of a rise in temperature followed by headache. Examination revealed enlargement of the spleen and swelling of the lymph glands, eosinophilia and jaundice, associated with a positive thymol turbidity test. Upon readministration of the drug, a rise in temperature, eosinophilia, and increased thymol turbidity values were again noted. Cutaneous tests with the drug gave negative reactions. H.

Cortisone in Allergic Purpura of Children. Kugelmass, I. N.: New York State J. Med. **51**: 2504, 1951.

Four cases of allergic purpura in children were observed. Two patients who developed symptoms of Henoch's purpura due to food allergy were treated with dietary restriction and cortisone. Gastrointestinal disturbances, purpuric manifestations, and increased capillary fragility as determined by the tourniquet test disappeared within 72 hours. The other 2 patients developed symptoms of Schönlein-Henoch's purpura due to streptococcal infection, one associated with acute glomerulonephritis and the other with rheumatic carditis. With cortisone therapy, the abdominal and joint pains as well as the purpura subsided within 96 hours. In 2 of the 4 children, thrombocytopenia associated with the purpura also responded to cortisone therapy. After withdrawal of cortisone, mild purpura recurred in the 2 cases of Schönlein-Henoch's purpura. Cortisone is regarded as the most effective therapeutic agent now available for repairing vascular injury. B. S.

Anaphylaxis

Effects of Cortisone on Tissue Electrolyte Changes During Anaphylactic Shock in the Mouse. Nelson, C. T., Fox, C. L., Jr., and Freeman, E. B.: J. Invest. Dermat. **18**: 113, 1952.

Mice were sensitized to horse serum by means of repeated intraperitoneal injections. The animals were shocked 11 to 15 days after the last sensitizing injection. Approximately half the animals were given 3 mg. of cortisone intramuscularly 18 to 24 hours prior to the challenging dose of antigen. Hematocrit and other determinations were made on blood specimens obtained from the hearts of the animals. Tissue electrolyte determinations were carried out on the amputated hind legs of the mice. Similar studies were made on

the bloods and hind legs of animals receiving an initial injection of horse serum 45 minutes before the collection of the specimens. None of the animals treated with 3.0 mg. of cortisone died in anaphylactic shock, whereas 73 per cent of the untreated mice died in shock. Mice receiving smaller doses of cortisone showed some degree of protection from fatal shock. The hematocrit values of animals dying in shock were much higher and the legs contained significantly more sodium and chloride than the cortisone-treated group or the normal animals which received an equivalent amount of horse serum. The potassium content of the legs of the shocked animals, however, was considerably less than that found in the control mice or in the cortisone-protected mice. The authors are not yet certain whether the electrolyte changes are of primary importance in anaphylaxis or whether they secondarily reflect changes occurring in cells as a result of the rapid union of antigen and antibody. R. W.

Pharmacology, Physiology, and Pathology

The Effect of Several New Antihistaminic Drugs Upon the Mammalian Capillary Bed. Haley, T. J., and Andem, M. R.: J. Pharmacol. & Exper. Therap. **100**: 393, 1950.

The mesoappendix capillary bed was studied microscopically in a live animal to determine the response of precapillary sphincters to various concentrations of 15 new antihistaminic drugs. Epinephrine and histamine checks were run on the same preparations. The antihistamines, employed in concentrations approximating those attained clinically, all caused constriction of the capillary bed. "In the dilutions which were effective, the degree of local vasoconstrictor activity of the drugs was equivalent to that observed after epinephrine application. All of the antihistaminic agents caused the leukocytes to adhere to the vessel walls, whereas histamine always caused the leukocytes to enter the streamline erythrocyte flow in the center of the vessels." Anthallan was the most potent of the antihistamines studied in vasoconstrictor activity. A new preparation, chloroprophenyyridamine was next in potency. Benadryl and Pyribenzamine were less active. Chemical structure and its relationship to vasoconstrictor activity is discussed. K.

The Relation of Pulmonary Arterial Pressure Variations to the Activity of Afferent Pulmonary Vascular Fibres. Pearce, J. W., and Whitteridge, D.: Quart. J. Exper. Physiol. **36**: 177, 1951.

Cats, sheep and goats were anesthetized, a cannula was inserted in the pulmonary artery and the chest wall was closed. The vagus nerve was dissected, severed and split into strands, and the peripheral ends were laid across electrodes of an amplifier. During spontaneous respirations, the pulmonary arterial pressure rose with inspiration and decreased during expiration. Maintained positive pressure inflation resulted in decreased pulmonary arterial pressure which promptly rose with release from the forced inflation. Maintained negative pressure deflation of the lungs brought about a rise in pulmonary arterial pressure which reverted to normal values when suction was stopped. In both of these instances aortic pressure showed similar changes but with a greater time-lag following the stimulus. It was possible to differentiate the sites or origin of various types of nerve fibers based on the timing of their discharges with relation to cardiac and respiratory rhythms. One group of pulmonary arterial nerve fibers discharged impulses related to pulmonary arterial pressure changes. Inflation of the lungs brought about cessation of these nerve discharges and decreased pulmonary arterial pres-

sure. Deflation of the lungs had the opposite effect. The correlation between pulse pressure and fiber activity was poor for aortic pressures. It is concluded that pulmonary vascular fibers arise from endings in the pulmonary circuit and are stimulated by distention of the vessel. The time factors involved suggest that the receptors may be on the arterial side of the pulmonary vascular bed. The function of these fibers remains unknown. K.

The Potentiating Effect of ACTH and of Cortisone on Pressor Response to Intravenous Infusion of L-Nor-Epinephrine. Kurland, G. S., and Freedberg, A. S.: Proc. Soc. Exper. Biol. & Med. **78**: 28, 1951.

The blood pressure response to an intravenous infusion of l-nor-epinephrine, administered with a constant rate infusion apparatus, was determined in 3 patients. The determinations were made before, during, and after the administration of ACTH or cortisone. Within 24 hours after hormone therapy was started, there was a striking potentiation of the pressor response to nor-epinephrine in all patients. This effect disappeared within 36 hours after the discontinuance of these agents. It is postulated that ACTH and cortisone sensitize the vasculature of man to endogenous nor-epinephrine. This may explain the frequent finding of elevation of blood pressure during such hormone therapy and may also explain the hypertension of Cushing's disease. B. S.

Electrocardiographic Changes Associated With Allergic Reactions to Penicillin. Binder, M. J., Gunderson, H. J., Cannon, J., and Rosove, L.: Am. Heart J. **40**: 940, 1950.

Transient electrocardiographic changes were observed in 3 patients at the height of severe serum sickness type reactions following penicillin therapy. In one case the T waves were inverted in Leads I, II, III and V_5 with return to normal in 5 days. In the second case, T_1 was isoelectric and T waves were inverted in Leads II, III, V_4, V_5 and V_6. Tracings became normal in about one week. In the third case, the abnormality noted was also inversion of the T wave. There were no complaints relative to the cardiovascular system. Similar findings have previously been reported in allergic reactions and have been attributed to serum carditis, anoxia, or transient pericarditis. No electrocardiographic abnormalities were found in 25 additional patients with mild drug sickness reactions. K.

The Effect of Cortisone on the Lesions of Periarteritis Nodosa. Baggenstoss, A. H., Shick, R. M., and Polley, H. F.: Am. J. Path. **27**: 537, 1951.

Two cases of periarteritis nodosa treated with cortisone came to necropsy. One patient received 3.6 grams of cortisone and was observed for 75 days, the other received 13.7 grams of the drug and was observed for 146 days. Despite initial improvement, both patients died of cardiac and renal failure.

Histologically, all signs of active inflammation had disappeared. Biopsies performed in both cases during the course of the disease had shown acute arteritis. There was complete healing of all arterial lesions with fibrous obliteration of these vessels, resulting in infarcts, which were numerous in the kidneys, heart, and intestinal tract. One case also showed aneurysm formation, thrombosis, and hemorrhage. In both instances, the adrenal cortex showed moderate atrophy and a decrease in lipoid content.

The histologic signs of healing, following cortisone therapy, were quite similar to the healing described in those cases in which spontaneous healing

occurred. It is considered significant that the healing in these 2 cases occurred more rapidly than has been previously reported. J. S.

Effect of Cortisone on Histamine Liberation Induced by Tween in the Dog. Goth, A., Allman, R. M., Merritt, B. C., and Holman, J.: Proc. Soc. Exper. Biol. & Med. **78**: 848, 1951.

Male dogs injected intravenously with Tween 20 at 24 or 48 hour intervals showed an increase in the plasma histamine as determined by paper chromatography and a resultant marked fall in blood pressure. The hypotensive response to the second Tween injection was less pronounced than that obtained with the first injection. Cortisone treatment was started on one group of male dogs prior to the first Tween injection and was continued for 24 or 48 hours. Cortisone had no effect on the hypotensive response to the first injection, but decreased or prevented the response to the second Tween injection. When the interval between injections was 48 hours, the cortisone-treated animals were completely refractory to the hypotensive action of the second injection of Tween 20. Histamine, administered intravenously to the dogs in the refractory phase, caused a marked fall in blood pressure. This interference with the Tween phenomenon by cortisone could not be clearly demonstrated in female dogs. It is suggested that cortisone prevents the resynthesis of histamine in the tissues following its release and/or stimulates the destruction of histamine in the tissues following the release of this compound by Tween 20. B. S.

Effect of Isuprel on Antigen-Antibody and Histamine Skin Reaction. Sheldon, J. M., Husted, J. R., and Lovell, R. G.: Ann. Allergy **9**: 45, 1951.

Isopropylepinephrine, known as Isuprel, Isonorin, or Aludrine, exerts an effect similar to epinephrine in the symptomatic relief of bronchial asthma. Prick and intracutaneous tests with allergens and histamine were performed on patients who received Isuprel sublingually or by inhalation. These studies revealed that Isuprel, like epinephrine, inhibits the degree of whealing response of the skin to intracutaneous tests. Little change was observed in the whealing response when the prick technique was used. The histamine-induced dermal reaction was not materially altered. The authors recommended withholding Isuprel prior to and during skin testing in order to prevent alteration of the test result. M. Scherr

The Effect of Khellin on Cardio-Pulmonary Function in Chronic Pulmonary Disease. Silber, E. N., Snider, G. L., Goldberg, H., Katz, L. N., and Radner, D. B.: J. Clin. Investigation **30**: 1046, 1951.

Six men with chronic silicosis, anthracosis, bronchiectasis, or emphysema were subjected to electrocardiographic study, right heart catheterization, and studies of respiratory gases in arterial blood and expired air at rest and during exercise. Khellin was administered intramuscularly and the investigations were repeated immediately thereafter. The drug was then administered orally for from 5 to 8 days and the subjects were again examined. Following the intramuscular injection, no consistent change was noted "during rest or exercise in ventilation, oxygen uptake, oxygen removal, cardiac output or pulmonary arterial pressure. . . ." Following the course of oral therapy, maximal breathing capacity was increased but there were "no consistent changes . . . in ventilation, oxygen uptake, oxygen removal, cardiac output or pulmonary arterial pressure. Khellin did not appear to have any protective effect on the arterial saturation during exercise." K.

Diphenhydramine Hydrochloride, U. S. P. XIV, and Respiratory Tract Fluid. Bidwell, S. M. R., and Boyd, E. M.: J. Pharmacol. & Exper. Therap. **104**: 224, 1952.

Respiratory tract fluid was collected through a T-cannula ligated in the trachea of rabbits, cats, guinea pigs, and rats which were kept in an air conditioning chamber. Hourly output of respiratory tract fluid was measured for 3 hours. Benadryl was then injected subcutaneously in various doses and further measures of respiratory tract fluid were taken. Control animals were also studied. The rate of volume output, chloride content, relative viscosity, and specific gravity of the respiratory tract fluid thus collected were unchanged following the administration of Benadryl. The amounts used varied from therapeutic doses to lethal doses. It is suggested that Benadryl and perhaps other antihistamines are useless additions to expectorant cough mixtures. These studies were made only on healthy animals. K.

Miscellaneous

The Action of Histamine and Antihistaminic Substances on the Endothelial Cells of the Small Capillaries in the Skin. Matoltsy, A. G., and Matoltsy, M.: J. Pharmacol. & Exper. Therap. **102**: 237, 1951.

The Jansco phenomenon was reproduced by painting the abdominal skin of rats with 1 per cent histamine for 10 minutes and then injecting India ink intravenously. Sections of painted skin were then removed after 1, 6, 24, and 48 hours for histologic study. Within one hour after the ink injection, the skin of the painted area was grossly black and carbon particles were adsorbed on the walls of the small capillaries of the dermis and subcutaneous tissue. After 6 hours, the carbon particles were found to be attached to both the surface and the inside of the endothelial cells. After 24 to 48 hours, carbon particles were still in endothelial cells and also had been taken up by histiocytes and fibrocytes around the small capillaries where they remained for as long as 4 months. The surrounding skin which had not been painted with histamine was unaffected. To determine the duration of the effect of histamine application on skin capillary phagocytosis, the backs of mice were painted with a 2 per cent histamine solution for 5 minutes and ink was injected intravenously at various intervals. Ink was adsorbed in the painted area when it was injected within 5 or 10 minutes following the histamine application, but adsorption was decreased after a 15 minute interval. If the ink was not injected within 30 minutes after painting the skin, there were no carbon particles adsorbed.

It was then found that the same area of skin could be histamine-painted repeatedly without prejudicing the uptake of carbon particles or influencing the time interval during which phagocytosis occurred. When the skin was traumatized with a surgical clamp, the endothelial cells actively adsorbed carbon particles for 2 hours and the effect could be detected for up to 20 hours. Benadryl, Pyribenzamine, and Neoantergan in various concentrations were mixed with the histamine and painted on the skin. With increasing antihistamine concentrations, progressively less carbon was fixed in the skin. Benadryl in 2 per cent aqueous solution painted on the skin for 5 minutes just before clamp injury and again immediately afterward for 2 minutes almost abolished carbon phagocytosis. Histamine was equally active in acid or in alkaline solution. Trauma to the skin by burning or freezing also induced the adsorption phenomenon. It is suggested that since skin capillary phagocytosis is an important defense mechanism and the antihistaminics inhibit this function at least in animals, their clinical application in local infections is questionable. K.

Acquired Resistance to the Shwartzman Phenomenon. Cluff, L. E., and Bennett, I. L.: Proc. Soc. Exper. Biol. & Med. **77**: 461, 1951.

Experiments designed to study resistance to the Shwartzman phenomenon were carried out on rabbits that had demonstrated typical hemorrhagic skin lesions. The materials employed to elicit the reactions consisted of the P-25 polysaccharide from Serratia marcescens and meningococcus culture filtrate. One group of these animals received repeated intracutaneous preparatory and intravenous provocative injections of the filtrate on alternate days. By the fourth set of injections, these rabbits failed to exhibit the Shwartzman phenomenon. Other groups were given either the intracutaneous preparatory injection or the intravenous provocative injection alone on alternate days. After the fourth injection, all of the animals in these groups failed to demonstrate the Shwartzman phenomenon. Control animals that received no injections for 8 days after the initial reaction manifested typical hemorrhagic skin lesions on being tested. The resistance induced in these animals was transient and disappeared after resting the animals for about 21 days. The resistance was overcome shortly after being induced by increasing the intravenous provocative dose five times, but could not be overcome by increasing the intracutaneous preparatory dose by a similar amount. Rabbits made resistant by injections with one filtrate were also resistant to other filtrates. After a rest period of about 3 weeks, the same animals demonstrated positive reactions with the heterologous filtrates. Attempts to transfer the resistance passively via serum to normal animals were unsuccessful. When serum from the resistant animals was added to the filtrates prior to injection it failed to inactivate them. B. S.

Enhanced Clinical Effectiveness of Purified Corticotropin. Raben, M. S., Rosenberg, I. N., Westermeyer, V. W., and Astwood, E. B.: J. A. M. A. **148**: 844, 1952.

An oxycellulose purified corticotropin was shown to contain 80 U.S.P. units per mg. by bio-assay. In a series of 18 patients, the aqueous solution of this purified hormone was shown to be about 150 times as effective clinically as the standard corticotropin and at least 250 times as effective as cortisone. This increased effectiveness allows for a significant reduction in the dosage requirements, i.e., asthmatic patients were benefited by from 40 to 60 U.S.P. units (0.5 to 0.75 mg.) per day, and patients with rheumatoid arthritis were controlled with as little as 0.19 mg. per day. The increased efficiency of this product may be due to a greater stability of the purified corticotropin in body fluids or to the possible presence in the cruder preparations of destructive contaminants, such as proteolytic enzymes. The increased efficiency could also result from removal, during purification, of physiologically antagonistic substances. F.

Effective Therapy of Severe Penicillin Reactions With Sodium Dehydrocholate: Clinical Studies of Liver Dysfunction—XII. Pelner, L., and Waldman, S.: Amer. Pract. **3**: 293, 1952.

Serum sickness-like reactions to penicillin were controlled in 14 cases by 4 or 5 daily intravenous injections of 5 c.c. sodium dehydrocholate combined with orally administered dehydrocholic acid. Antihistaminics and epinephrine were sometimes used as adjuvants in the treatment. It is postulated that the effectiveness of this medication lies in its ability to depress some of the liver functions without causing actual liver damage. Dehydrocholic acid is an

oxidized derivative of cholic acid and bears some similarity chemically to cortisone. In the authors' opinion, this acid may be a starting point for the in vivo synthesis of cortisone. F.

Ingestion of 1250 Mg. of Demerol (Isonepecaine) With Suicidal Intent. A Case Report. Cohen, A. E.: Ann. Allergy **8**: 547, 1950.

Demerol poisoning was observed in a 34-year-old white man with bronchial asthma and bronchiectasis who swallowed 1250 mg. of the drug with suicidal intent. Thirty minutes after consuming the drug, he vomited. Toxic symptoms, while minimal, consisted of drowsiness and confusion. The patient was treated with Benzebar and gastric lavage. Although his asthma became slightly worse 24 hours after the suicidal attempt, it responded to therapy with aminophyllin and expectorants. Recovery was complete. E. W.

Eosinophilic Granuloma of the Stomach and Small Intestine. Booher, R. J., and Grant, R. N.: Surgery **30**: 388, 1951.

A 57-year-old white female with gastrointestinal symptoms and x-ray evidence of a pyloric tumor was subjected to laparotomy. The lesion proved to be an eosinophilic granuloma of the stomach and small intestine. Microscopic examination revealed marked infiltration of fibrocytes and eosinophiles into the submucosa. The blood eosinophilia was only 2 per cent. The family history was positive for allergy, but allergic studies performed on the patient gave negative findings. Eleven additional cases previously reported in the literature were reviewed. Two of these cases showed a blood eosinophilia which varied from 18 to 31 per cent. J. S.

Procaine Amide. A Clinical Study. Sadove, M. S., Wyant, G. M., and Kretchmer, H. E., and Gittelson, L. A.: Current Researches in Anesth. & Analg. **31**: 45, 1952.

Procaine is the hydrochloride salt of the ester of para-aminobenzoic acid with diethylaminoethanol. Procaine amide is obtained by replacing the ester link with an amide group.

Procaine amide has no stimulatory effect on the central nervous system and has a more prolonged analgesic effect than procaine. Procaine amide can be administered orally. Fewer cases of hypotension result when the amide is given. The amide does not disturb normal liver or kidney function and has no effect on the sedimentation rate and blood count. Pyloric spasms, pruritus, and the pain of myositis and fibrositis are adequately relieved by the amide. H.

Streptococcal Bacteriostatic Antibody in Patients Treated With Penicillin. Daikos, G., and Weinstein, L.: Proc. Soc. Exper. Biol. & Med. **78**: 160, 1951.

Patients with scarlet fever from whom the beta-hemolytic streptococcus was isolated within 24 hours of admission were studied. Serum drawn before and after the onset of penicillin therapy was examined for type specific bacteriostatic antibody, antihyaluronidase, and antistreptolysin 0 titers. There was an inverse relationship between the dose of penicillin administered and the amount of bacteriostatic antibody developed. When large doses of penicillin were administered, no type specific bacteriostatic antibody was found. Lower bacteriostatic antibody titers were obtained following the intramuscular route of administration of penicillin than resulted from the oral route of ad-

ministration. When present, bacteriostasis became evident between the third and fifteenth week after the onset of infection and persisted for at least 15 weeks. The findings seemed to indicate that the administration of penicillin not only may inhibit completely the development of bacteriostatic antibody but may also decrease the amount developed and shorten the duration of the period during which it is detectable. No relationship existed between the antihyaluronidase, antistreptolysin 0, and bacteriostatic antibody titers. Penicillin probably suppresses antibody formation because of the rapid removal of the antigenic focus. It is suggested that certain penicillin dosage schedules actually depress the development of effective immunity and increase the risk of subsequent infection by homologous serological types. B. S.

Prevention of Allergic Transfusion Reactions: The Prophylactic Use of Antihistamine in Blood to Prevent Allergic Transfusion Reactions. Ferris, H. E., Alpert, S., and Coakley, C. S.: Amer. Pract. **3**: 177, 1952.

In a series of 367 patients who had received a total of 607 transfusions to which 25 mg. of Pyribenzamine per pint had been added, there was only one allergic reaction (0.16 per cent) and there were no pyrogenic reactions. Among a control series, patients who had been given 742 pints of blood without Pyribenzamine, there were 20 allergic reactions (2.69 per cent) and 32 pyrogenic reactions (4.31 per cent). One hemolytic reaction was encountered in the entire series and this occurred in a patient who received blood to which Pyribenzamine had been added. The fact that there were no pyrogenic reactions among the experimental series suggests that such reactions may be due to histamine liberation. F.